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PATENT 00 1290 Docket No.: 19603/4071 (CRE) 05-13-598-47

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Vivian E. Mack Strong, et al. Examiner: Unknown Serial No. 09/782,936 Art Unit: Cnfrm. No.: 1665 1614 Filed February 14, 2001 **USE OF COX-2 INHIBITORS TO TREAT** For SEPSIS AND COMPLICATIONS THEREOF, AND EP RECEPTOR MODULATION

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §§ 1.97-1.98

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

Pursuant to 37 CFR §§ 1.97-1.98, applicants hereby bring to the attention of the United States Patent and Trademark Office, the enclosed references listed on the attached PTO-1449 form.

- 1. Andrews N.C. and Faller D.V., A rapid micropreparation technique for extraction of DNA-binding proteins from limiting numbers of mammalian cells. *Nucleic Acids Research* 19(9):2499, 1991.
- 2. Baker, C.C., Oppenheimer, L., Stephens, B., Lewis, F.R., and Trundey, D.D. Epidemiology of trauma deaths. *Am. J. Surg.* 140: 144, 1980.
- 3. Boyum, A., Isolation of mononuclear cells and granulocytes from human blood. *Clin. Lab. Inves. Supp. 21*:77-79, 1968.
- 4. Ertel, W., Singh, G., Morrison, M.G., Ayala, A., and Chaudry, I.H. Chemically induced hypotension increases PGE₂ release and depresses macrophage antigen presentation. *Am. J. Physiol.* 264: R655, 1993.

- 5. Faist, E., Mew, A., Baker, C.C., Strasser, T., Alkan, S.S., and Rieber, P., Heberer, G. Prostaglandin E2 (PGE₂)-dependent suppression of interleukin-2 production in patients with major trauma. *J. Trauma*. 27: 837, 1987.
- 6. Fletcher, J.R., and Ramwell, P.W. Indomethacin improves survival after endotoxin in baboons. *Adv. Prostaglandin. Thromboxane Res.* 7: 821, 1980.
- 7. Fukushima, R., Alexander, J.W., Wu, J.Z., and Mao, J.X., Szczur, K., Stephens, A.M., Ogle, J.D., Ogle C.K. Time course of production of cytokines and prostaglandin E2 by macrophages isolated after thermal injury and bacterial translocation. *Circ. Shock.* 42: 154, 1994.
- 8. Futaki, N., Takanashi, S., Yokohama, M., Arai, I., Higuchi, S., and Otomo, S. NS-398, a new antiinflammatory agent, selectively inhibits prostaglanding G/H synthase/cyclooxygenase (COX-2) activity *in vitro*. *Prostaglandins*. 47: 55, 1994.
- 9. Gabay, D., and Kushner, I. Acute-phase proteins and other systemic resonses to inflammation. *N. Engl. J. Med.* 340: 448, 1999.
- 10. Grbic, J.T., Mannick, J.A., Gough, D.B., and Rodrick, M.L. The role of prostaglandin E2 in immune suppression following injury. *Ann. Surg.* 214: 253, 1987.
- 11. Hinshaw, L.B., Solomon, L.A., Erdos, E.F., Reins, D.A., and Gunter, B.J. Effects of acetylsalicylic acid on the canine response to endotoxin. *J. Pharmacol. Exp. Ther.* 157: 665, 1967.
- 12. Hinson, R.M., Williams, J.A., and Shacter, E. Elevated interleukin 6 is induced by prostaglandin E2 in a murine model of inflammation: possible role of cyclooxygenase-2. *Proc. Natl. Acad. Sci. U.S.A.* 93: 485, 1996.
- 13. Lin, E., Calvano, S.E., and Lowry, S.F. Inflammatory cytokines and cell response in surgery. *Surgery*. 127: 117, 2000.
- 14. Mack, V., McArter, M.D., Naama, H.A., Calvano, S.E., Daly, J.M., Dominance of T-Helper 2-type cytokines after severe injury. *Arch. Surg.* 31:1303-1309, December, 1996.
- 15. Mack Strong et al., "Blocking Prostaglandin E₂ After Trauma Attenuates Pro-Inflammatory Cytokines and Improves Survival," *Shock*, Vol. 14, No. 3: 374-379 (2000).

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- 16. Mack, V.E., et al. "Blocking Prostaglandin-E2 after Trauma is Associated with decrease Cox-2 mRNA Expression and Survival," abstract published April 20, 2000, Annual Meeting of the Surgical Infection Society.
- 17. Mack, V.E., et al. "Trauma Induces Prostaglandins and Cox-2 mRNA in Human and Experimental Models. Could Cox-2 Inhibitors be the Cure?" abstract, published April 20, 2000, Annual Meeting of the Surgical Infection Society.
- 18. McCarter, M.D., Mack, V.E., Daly, J.M., Naama, H.A., Calvano, S.E. Trauma-induced alterations in macrophage function. *Surgery*. 123: 96, 1998.
- 19. O'Sullivan, S.T., Lederer, J.A., Horgan, A.F., Chin, D.H.L., Mannick, J.A., and Rodrick, M.L. Major injury leads to predominance of the T helper-2 lymphocyte phenotype and diminished interleukin-12 production associated with decreased resistance to infection. *Ann. Surg.* 222: 482, 1995.
- 20. Parratt, J.R., and Sturgess, R.M. *E. coli* endotoxin shock in the cat: treatment with indomethacin. *Br. J. Pharmacol.* 53: 485, 1975.
- 21. Rangel-Fausto MS et al., (1995) "The natural history of the systemic inflammatory response syndrome (SIRS): a prospective study. *JAMA 273*:117-23.
- 22. Rangel-Fausto MS et al., "Increases in National Hospital Discharge Survey Rates for Septicemia- United States, 1979-1987: *Morb. Mortal. Wkly Rep. 39*:31-4, 1990."
- 23. Vane, J.R. Inhibition of prostaglandin synthesis as a mechanism oaf action for aspirin-like drugs. *Nature (London)*. 231: 232, 1971.
- 24. Versteeg, J.J., van Vergen en Henefouwen, P.M.P., van Deventer, S.J.H., and Peppelenbosch, M.P. Cyclooxygenase-dependent signaling: molecular events and consequences. *FEBS Lett.* 445:1, 1999.
- 25. Zellweger, R., Ayala, A., Zhu, X.L., Morrison, M.H., and Chaudry, I.H. Effect of surgical trauma on splenocyte and peritoneal macrophage immune function. *J. Trauma*. 39: 645, 1995.
 - 26. U.S. Patent No. 5,633,272 to Talley et al., issued May 27, 1997
 - 27. U.S. Patent No. 5,731,343 to Feng et al., issued March 24, 1998.
 - 28. U.S. Patent No. 5,905,089 to Hwang et al., issued May 18, 1999.
 - 29. U.S. Patent No. 6,048,850 to Young et al., issued April 11, 2000.
- 30. International Patent Application WO 99/30721 A1, published June 24, 1999.

Copies of each of the references are also provided herewith. All of the references are in the English language.

Consideration of this Information Disclosure Statement is respectfully requested, since the art provided may be material to the examination of the present invention as defined in 37 C.F.R. § 1.56(a).

Inasmuch as this Information Disclosure Statement is being submitted prior to the issuance of an Official Action on the merits, no fee, certification or petition is required by Applicants.

Respectfully submitted,

Date: June 5, 2001

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)

I certify that the attached correspondence is being deposited on 6/5/0/ with the U.S. Postal Service as first class mail under 37 C.F.R. § 1.8 and addressed to:

Assistant Commissioner for Patents, Washington, D.C. 202

Maria L Maton